REMARKS

Claims 1-20 were pending in this application when last examined. Claims 11 and 12 are cancelled, claims 1-10 and 13-20 are currently amended, and new claims 21-24 are added.

Support for the amendments can be found in the specification and original claims as filed. No new matter has been added. Support for non-steroidal anti-inflammatory drugs (NSAID) can be found, for example, in paragraphs [0079], [0080] and [0090], as referenced in the patent application publication (US 2007/0110801 A1).

CLAIM REJECTIONS – 35 USC § 101

At page 2, item 5, the Office Action rejects claims 11 and 12 under 35 U.S.C. § 101, as not being proper process claims. Applicants respectfully traverse the rejection.

Claims 11 and 12 have been cancelled. New claims 21 and 22 address the issues in this rejection. Claims 21 and 22 are each directed to a method that sets forth positive steps. Each of claims 21 and 22 satisfies the requirements of 35 U.S.C. § 101. Accordingly, Applicants request reconsideration and withdrawal of the rejection.

CLAIM REJECTIONS – 35 USC § 112, FIRST PARAGRAPH

At page 3, item 7, the Office Action rejects claims 9 and 10 under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. Applicants respectfully traverse the rejection.

The Office Action states that "metolose" is not described in the specification as to what it actually is. One of ordinary skill in the art would recognize that metolose is a type of methyl cellulose. More specifically, metolose is a hydroxy-propyl methyl cellulose having the formula $C_{32}H_{60}O_{19}$. The IUPAC name is 2-[6-[4,5-bis(2-hydroxypropoxy)-2-(2-hydroxypropoxymethyl)-6-methoxyoxan-3-yl] oxy-4,5-dimethoxy-2-(methoxymethyl)oxan-3-yl]oxy-6-(hydroxylmethyl)-5-methoxyoxane-3,4-diol.

The specification further discloses, for example at paragraphs [0042]-[0047], that the composition can include cellulose derivatives, such as carboxy-methyl and hydroxy-propyl methyl cellulose. At paragraphs [0079] and [0080], Applicants disclose embodiments of the composition that include metolose as a type of hydroxy-propyl methyl cellulose.

Finally, currently amended claims 9 and 10 no longer recites metolose. Amended claims 9 and 10 feature hydroxy-propyl methyl cellulose in the composition.

Thus, claims 9 and 10 satisfy the requirements of 35 U.S.C. § 112, first paragraph. Accordingly, Applicants request reconsideration and withdrawal of the rejection.

CLAIM REJECTIONS – 35 USC § 112, SECOND PARAGRAPH

At page 3, item 9, the Office Action rejects claims 1-3 and 9-13 under 35 U.S.C. § 112, second paragraph, as being indefinite. Applicants respectfully traverse the rejection.

Regarding claims 1-3 and 13, the Office Action holds the position that "derivative of the aryl-carboxylic family" is indefinite. Currently amended claims 1-3 and 13 no longer recite the "derivative" terminology in question.

Regarding claims 9 and 10, the Office Action states that the claims cannot recite the METOLOSE® trademark as a limitation to identify or describe a particular material or product. Currently amended claims 9 and 10 no longer recite metolose. The claims feature hydroxy-propyl methyl cellulose.

Regarding claims 11 and 12, the Office Action states that the claims fail to set forth any steps involved in the method. Claims 11 and 12 have been cancelled. New claims 21 and 22 are each directed to a method that sets forth clear positive steps. Claim 21 clearly encompasses a method for producing a medication, and claim 22 clearly encompasses a method for treating buccopharyngeal ailments.

In view of the amendments and the foregoing remarks, each of claims 1-10 and 13-24 satisfies the requirements of 35 U.S.C. § 112, second paragraph. Accordingly, Applicants request reconsideration and withdrawal of the rejection.

CLAIM REJECTIONS - 35 USC § 102

FINIDORI et al.

At page 5, item 14, the Office Action rejects claims 1-8 and 11-20 under 35 U.S.C. § 102(b) as being anticipated by FINIDORI et al. (US 6,056,944). Applicants respectfully traverse the rejection.

Currently amended independent claim 1 is directed to a composition to be administered as a tablet or lozenge, comprising a low dosage lipophilic non-steroidal anti-inflammatory (NSAID) or anti-mycotic drug under an amino acid salt form, wherein the composition can be passively diffused into buccal and throat mucous membranes when the composition is totally released, dissolved, coated to the mucous membrane, and then absorbed through the mucous.

Applicants have developed a composition wherein lipophilic compounds, such as nonsteroidal anti-inflammatory drugs and anti-mycotic drugs, can dissolve and remain stabilized while passively diffusing into the mucous membrane. The composition is effective toward buccal and throat mucous membranes, and is targeted for locally active therapies against

buccal pain and inflammation, e.g., aphtosis, gingivitis, and sore throat.

Previous attempts at developing similar compositions have been difficult. NSAID molecules are lipophilic, hydrophobic and insoluble in the mouth/saliva environment. As a result, the lipophilic molecules remain in the crystalline state and do not dissolve, and therefore, the active ingredient cannot be absorbed by the mucous epithelium. Moreover, the acid insoluble crystal forms induce nausea and local irritation when the drug comes in contact with mucous tissue.

Applicants have developed a way for lipophilic molecules to be absorbed by the permucosal route. The molecules being lipophilic would then have a straight local pharmacodynamic activity if absorbed by the mucous. Applicants solved the limiting condition of their pharmacological efficiency in regard to their solubility.

The claimed composition allows for lipophilic molecules to be “fleetingly” soluble in the aqueous environment of the mouth. The solubility is derived from low dosages of drug, which reduces the saturation risk, and using amino acid salt forms of these compounds, such as lysine, arginine or histidine salts. This composition provides for the liberation of active molecules in an aqueous environment, which are then turned back into a basic lipophilic structure when the molecule dissociates from the amino acid salt. Fleetingly turned back into its lipophilic

state, the molecules are available to be passively absorbed by the mucous membrane, but only if the molecule is maintained as dissolved and in close contact with the mucous.

Applicants developed a hygroscopic matrix, based on a highly hygroscopic polyol substrate, associated with specific polymers such as hydroxy-methyl cellulose, hydroxy-ethyl cellulose, hydroxy-propyl cellulose, hydroxy-propyl methyl cellulose, or carboxy-methyl cellulose, or their salts, or with gums such as guar gum, xanthane, or gum Arabic, or with other polymeric structures such as alginic acid and derivatives, carboxy-vinyl polymer, carbomer, macrogols, polyethylene glycols, gelatin, povidone, or pectins. This association with a polymer keeps the lipophilic molecule still dissolved while maintained on the lipophiic mucous membrane, and in this way, it allows the molecule to be instantaneously absorbed into the mucous depth.

The claimed composition provides for local, regular absorption and pharmacological activity in situ. The presently claimed composition includes at least two advantages that are not taught or suggested by the prior art.

The first advantage is to very slowly and progressively release the lipophilic molecule, at the same time dissolving in the mouth and locally coating the mucous, such that it is passively absorbed through the membrane within a few seconds. The low dosage drug can act locally, for example, against the intra-mucousal inflammation and pain.

The second advantage is that this instant dissolving and mucous coating technology is able to keep the lipophilic drug dissolved and in contact (i.e., "glued") with the mucous. This means that the drug is not diluted and swallowed into the salivary flow, which would then lead to the drug being removed from the local treatment area and ineffectively reaching the digestive tract.

Turning now to the cited references, FINIDORI fails to teach or suggest any composition having the combination of features as recited in the instant claims. FINIDORI relates to a lipid composition for conveying an active agent into a target cell. The composition is nothing like the instantly claimed composition.

The FINIDORI composition is an injectable, intra-articular, topical or ingestable aqueous emulsion (*see*, Abstract). The FINIDORI composition can be used, for example, in the form of toothpaste, mouthwash and gels (*see*, column 2, lines 6-8). In contrast to FINIDORI, instant claim 1 is directed to a composition to be administered as a tablet or lozenge.

The FINIDORI emulsion comprises a polar lipid mixture rich in phospholipids, in glycolipids and in ceramides, having a composition which is substantially similar to that of the polar lipid constituents of the cytomembranes of cells (*see*, Abstract). The ceramides are crucial to the FINIDORI composition. The ceramides enable the active agent (NSAIs) to be vectorized, that

is they improve the availability of the NSAIs at the site of action (*see*, column 1, lines 31-33). The ceramides employed are in the form of an aqueous emulsion whose oily phase consists of ceramides and of other lipids (*see*, column 1, lines 65-67). Again, the FINIDORI could not be administered as a tablet or lozenge, but is designed to be a liquid or gel.

For at least these reasons, FINIDORI fails to teach or suggest, and fails to anticipate, a composition having each and every feature recited in claim 1, and in claims 2-8, 13-20, and new claims 21-24 dependent thereon. Claims 11 and 12 have been canceled. Accordingly, Applicants request reconsideration and withdrawal of the rejection.

PANKHANIA et al.

At page 6, item 15, the Office Action rejects claims 1-8 and 11-20 under 35 U.S.C. § 102(b) as being anticipated by PANKHANIA et al. (WO 02/083119 A1). Applicants respectfully traverse the rejection.

PANKHANIA relates to a composition for treating migraine and nausea that includes ibuprofen and prochlorperazine. PANKHANIA speculates that in a composition comprising ibuprofen and prochlorperazine, the presence of prochlorperazine may increase the rate of absorption of ibuprofen by the body.

The PANKHANIA composition is taken by oral route and then metabolized to allow the active ingredients to reach the

brain blood flow be pharmacologically effective. It is strictly the typical systemic application of a drug combination against migraine and nausea using the combination of ibuprofen and prochlorperazine.

In contrast to PANKHANIA, instant claim 1 includes low dosages of lipophilic non-steroidal anti-inflammatory or anti-mycotic drugs formulated to be passively diffused into buccal and throat mucous membranes. Furthermore, instant claim 2 further includes a substrate that makes possible a slow permucosal diffusion that is uniform and localized to the buccopharyngeal cavity. As detailed above, the present composition relates to a locally slow releasing tablet or lozenge which allows the lipophilic drug to be fleetingly dissolved in the mouth environment, coated to the mucous, and be passively absorbed.

PANKHANIA utilizes from 50 to 800 mg of racemic ibuprofen in each dose (*see*, page 2, lines 28-31). These are high dosages related to a typical systemic application range. In contrast to PANKHANIA, the low dosage anti-inflammatory or anti-mycotic drug, as detailed in paragraphs [0079] and [0080], and as featured in claim 1, when used in a strictly local application, requires about 25 mg of ibuprofen per dosage, which then correlates to about 14.6 mg of racemic ibuprofen.

Furthermore, the high dosages of ibuprofen used in the PANKHANIA composition, even when as little as the lowest 50 mg dosage, would recrystallize in the mouth environment and thus

encounter the problems detailed in the comments above. The PANKHANIA composition would not work in a composition to be passively diffused into buccal and throat mucous membranes as recited in claim 1.

For at least these reasons, PANKHANIA fails to teach or suggest, and fails to anticipate, a composition having each and every feature recited in claim 1, and in claims 2-8, 13-20, and new claims 21-24 dependent thereon. Claims 11 and 12 have been canceled. Accordingly, Applicants request reconsideration and withdrawal of the rejection.

CLAIM REJECTIONS - 35 USC § 103

At page 7, item 17, the Office Action rejects claims 9-10 under 35 U.S.C. § 103(a) as being unpatentable over PANKHANIA, in view of MITRA (WO 95/07103). Applicants respectfully traverse the rejection.

Currently amended claims 9 and 10 are directed to a low dosage tablet according to claim 1, comprising a specific formulation. The formulation includes 25 mg of ibuprofen lysinate (claim 9) and 5 mg of ketoprofen lysinate (claim 10).

The Office Action acknowledges that PANKHANIA fails to teach or suggest a composition having these low dosages and relies on MITRA for teaching these dosage levels.

Like PANKHANIA, MITRA relates to a systemic compound to be administered by an oral route, with general effects on the

body and organs. MITRA describes a multi-ingredient and polyvalent systemic therapeutical application for treating the cold and flu, i.e, treating the throat, lungs, nasal congestion, bronchial secretions, etc. MITRA, however, fails to teach or suggest a strictly topical effect by locally releasing low dosage lipophilic anti-inflammatory or anti-mycotic drugs that are passively diffused into buccal and throat mucous membranes. In distinction from MITRA, the formulations of claims 9 and 10 relate to the localized delivery of low dosages of lipophilic anti-inflammatory or anti-mycotic drugs that are passively diffused into buccal and throat mucous membranes when totally released, dissolved, coated to, and then absorbed through mucous. The compositions of claims 9 and 10 can block local intra-mucous inflammation mechanisms such as cyclo-oxygenase enzymes and prostaglandins.

For at least these reasons, the combination of PANKHANIA and MITRA fails to teach or suggest, and would not have rendered obvious, the low dosage tablets of claims 9 and 10. Accordingly, Applicants request reconsideration and withdrawal of the rejection.

CONCLUSION

Having addressed each of the issues noted in the Office Action, the present application is in condition for allowance and notice to that effect is respectfully requested.

Should there be any matters that need to be resolved in the present application, the Examiner is respectfully requested to contact the undersigned at the telephone number listed below.

Please charge the fee of $52.00 for the 2 extra dependent claims being paid online simultaneously herewith by credit card.

The Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 25-0120 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17.

Respectfully submitted,

YOUNG & THOMPSON

/H. James Voeller/

H. James Voeller, Reg. No. 48,015
Customer No. 00466
209 Madison Street, Suite 500
Alexandria, VA 22314
Telephone (703) 521-2297
Telefax (703) 685-0573
(703) 979-4709

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APPENDIX:

The Appendix includes the following item(s):

☒ - a new or amended Abstract of the Disclosure